

variation from day to day in the common manner that occurs with cellular assays; most of this difference appeared to be related to differences in cell health or activity state following cell division. The assays were carried out using a coplanar waveguide apparatus described in detail in a co-filed application filed on even date herewith (entitled "Coplanar Waveguide Biosensor for Detecting Molecular or Cellular Events;" Attorney Docket No. 25US). Measurements were made over the range from 50 MHz to 1 GHz using SP21 (a two-port biosensor for measuring transmission loss) and SP11 (a one-port biosensor for measuring return loss) detectors, both gold and platinum chips, with  $5 \times 10^4$  cells/well plated the day before and using a sucrose buffer containing 1.26 mM  $\text{CaCl}_2$ , 0.81 mM  $\text{MgSO}_4$ , 5.37 mM KCl, 1 mM  $\text{MgCl}_2$ , 5 mM NaCl, 10 mM Hepes, 16 mM glucose, and 230 mM sucrose.

**Claims:**

This listing of claims will replace all prior versions and listings of claims in the application. Please amend the above-identified application as follows:

**Listing of Claims:**

1-10 (canceled)

11. (currently amended) A method of assaying cellular activity by monitoring a change in a cellular system, comprising:

coupling an electromagnetic test signal to a sample in which a cellular event is being detected, whereby said sample interacts with and modulates said test signal to produce a modulated test signal;

detecting said modulated test signal; and

analyzing said modulated test signal to detect said cellular event,

whereby said sample is coupled to said signal by a one-port coplanar waveguide transmission line operable to support the propagation of a an electromagnetic test signal, comprising:

a signal line ~~configured to conduct~~ capable of conducting a time-varying voltage therealong; and

one or more ground elements ~~configured to maintain~~ capable of maintaining a time-invariant voltage therealong, the one or more ground elements spaced apart from the signal line and located generally within the same plane as the signal line, wherein a detection region is formed

between a portion of the signal line and a portion of at least one of the one or more ground elements; and

whereby said sample is contained in a sample containment structure intersecting the detection region of the one-port coplanar waveguide transmission line, wherein the sample containment structure comprises a cavity operable to hold 1 ml or less of sample solution within the detection region; ~~and~~ ; and

whereby said sample contains at least one cell, said at least one cell being plated in the sample containment structure.

12. (currently amended) The method of claim 11, wherein said cellular activity comprises a change in amount of a cellular substance present in said at least one cell as the result of presence of a test substance in a medium containing said at least one cell.

13. (currently amended) The method of claim ~~11~~ 12, wherein said cellular substance is a protein, a lipid, a carbohydrate, a nucleic acid, water, or an ion.

14. (original) The method of claim 11, wherein said cell comprises artificially inserted genetic material encoding a target receptor.

15. (currently amended) The method of claim 11, wherein said at least one cell is a wild-type cell.

16. (currently amended) The method of claim 12, wherein said at least one cell comprises a receptor having a known activity and said change results from activity of said test substance as an agonist or antagonist of said receptor activity.

17. (original) The method of claim 11, wherein said change is opening or closing of an ion channel.

18. (currently amended) The method of claim 11, wherein said at least one cell is a mammalian cell.

19. (currently amended) The method of claim 18, wherein said at least one cell is a CHO cell.

20. (original) The method of claim 11, further comprising verifying said method by correlating with a known cell activity of a known substance prior to testing an unknown substance.

**Remarks:**

The Applicant respectfully submits the amendments above and the following remarks in response to the Office action mailed 25 March 2004.

I. Response to claim rejections under 35 U.S.C. 112

Claims 11-20 were rejected under 35 U.S.C. 112 as being indefinite. Claims 11-20 have been amended to clarify the claimed subject matter. Claim 11 has been amended to more clearly note that the applicant is claiming a signal line that is capable of conducting a time-varying voltage, as well as one or more ground elements that are capable of maintaining a time invariant voltage. The signal line's capability to conduct a time-varying voltage is based on the inherent physical properties of the chosen line and does not require any other means of preparation. The ground element's ability to maintain a time-invariant voltage is based on the physical properties of the chosen ground elements and does not require any additional method steps. The amendment does not introduce new matter.

The limitation "said cell" recited in claims 12, 15, 16, 18, and 19 has been given sufficient antecedent basis by the additional amendment to the last line of claim 11: "whereby said sample contains at least one cell, said cell being plated in the sample containment structure."

Support for this amendment can be found in paragraph [0070]:

Measurements were made over the range from 50 MHz to 1 GHz using SP21 (a two-port biosensor for measuring transmission loss) and SP11 (a one-port biosensor for measuring return loss) detectors, both gold and platinum chips, with  $5 \times 10^4$  cells/well plated the day before and using a sucrose buffer containing 1.26 mM  $\text{CaCl}_2$ , 0.81 mM  $\text{MgSO}_4$ , 5.37 mM KCl, 1 mM  $\text{MgCl}_2$ , 5 mM NaCl, 10 mM Hepes, 16 mM glucose, and 230 mM sucrose.

Claim 13 has been amended to depend from claim 12 and the limitation “said substance” has been given sufficient antecedent basis by amending claim 12 to clarify that the discussed ‘substance’ was a cellular substance and to distinguish the cellular substance from the test substance. This amendment does not introduce new matter and support for the amendment can be found in the context of claims 11 and 12.

## II. Claim Rejections under 35 U.S.C. 102(e)

Claims 11-13, 16, 17, and 20 were rejected under 35 USC 102(e) as being anticipated by Bodner et al. (U.S. 6,461,808). Applicant respectfully disagrees with the Examiner that applicant’s claims are anticipated by Bodner et al. The Examiner stated that Bodner et al., in claim 7, teach a method where the sample is coupled to the signal by a one-port coplanar waveguide transmission line operable to support the propagation of an electromagnetic test signal. Applicant respectfully disagrees. In Bodner et al.’s claim 7, they teach the use of a coaxial line. In having a cylindrical shape, a coaxial line has a completely different shape than a flat coplanar waveguide. Bodner et al. note that coplanar waveguides and coaxial cables are different transverse electromagnetic transmission structures in column 5, lines 24-32. Because cells will settle in a solution, Bodner’s patent allows the measurement of cellular events with cells suspended in solution but not cells that are settled or plated at the bottom of a containment structure, as taught by this application. Cells that are plated in a containment structure require the flat surface of a coplanar waveguide so that the sample solution containing the cells can pass above the measurement probe (as shown in Fig. 6). Bodner et al. do not teach a coplanar waveguide. The coaxial line that they teach is not analogous to a coplanar waveguide and will not allow the same experiments as a coaxial waveguide. Claim 11 additionally requires the plating of the at least one cell in the containment structure. A cell cannot be plated inside a pipette tip. Because the limitations of a coplanar waveguide and the plating of cells in the containment structure are not met by Bodner, applicant respectfully notes that applicant’s claims are not anticipated by Bodner. Because claims 12, 13, 16, and 17 depend from claim 11 and Bodner does not teach the limitations of claim 11, Applicant respectfully requests reconsideration of claims 11-13, 16, 17, and 20.

Claims 11-14, 16, and 18 were rejected under 35 USC 102(e) as being anticipated by Hefti et al. (U.S. 6,368,795). Hefti does not teach a method comprising the steps of coupling an electromagnetic test signal to a sample in which a cellular event is being detected in claim 1; Hefti et al. teach a method of coupling an electromagnetic test signal to a sample in which a molecular event is being detected. A molecular event is not a cellular event. The term 'cellular event' refers not only to reactions but to cellular living functions, structural rearrangements, and morphological changes (which often cannot be directly linked to a particular chemical reaction and which often occur down stream of a cascading series of events which may have been started by a molecular event). Hefti et al. are not detecting cellular events and do not teach the limitation of having at least one cell being plated in a sample containment structure. Applicant respectfully requests reconsideration of claims 11-14, 16, and 18.

### III. Claim Rejections under 35 U.S.C. 103

Applicant respectfully disagrees with the Examiner that applicant's claims are anticipated by Bodner et al. in view of Zang-Gandor [Zang-Gandor, Improved transfection of CHO cells, 1997, QIAGENnews, 4, 15-18] because all of the applicant's claim limitations are not met by the combination of Bodner et al. in view of Zang-Gandor (as discussed above).

Applicant respectfully disagrees with the Examiner that applicant's claims are anticipated by Hefti et al. in view of Zang-Gandor because all of the applicant's claim limitations are not met by the combination of Hefti et al. in view of Zang-Gandor (as discussed above).

### IV. Nonstatutory Double Patenting Claim Rejections

Claims 11-13, 16, 17, and 20 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,461,808. Applicant respectfully disagrees and notes that, as the Examiner stated, the claims are not identical. Because all of the applicant's claim limitations are not met by Bodner et al. [U.S. 6,461,808] (as discussed above), applicant reasserts that the claims are patentably distinct from each other and requests reconsideration of claims 11-13, 16, 17, and 20.

Claims 15, 18, and 19 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,461,808 in view of Zang-Gandor. Applicant respectfully disagrees and notes that, as the Examiner stated,

the claims are not identical. Because all of the applicant's claim limitations are not met by Bodner et al. [U.S. 6,461,808] (as discussed above) in view of Zang-Gandor, applicant reasserts that the claims are patentably distinct from each other and requests reconsideration of claims 5, 18, and 19.

Claims 11-14, 16, and 18 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 6,368,795. Applicant respectfully disagrees and notes that, as the Examiner stated, the claims are not identical. Because all of the applicant's claim limitations are not met by Hefti et al. [U.S. 6,368,795] (as discussed above), applicant reasserts that the claims are patentably distinct from each other and requests reconsideration of claims 11-14, 16, and 18.

Claims 15 and 19 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 6,368,795 in view of Zang-Gandor. Applicant respectfully disagrees and notes that, as the Examiner stated, the claims are not identical. Because all of the applicant's claim limitations are not met by Hefti et al. [U.S. 6,368,795] (as discussed above) in view of Zang-Gandor, applicant reasserts that the claims are patentably distinct from each other and requests reconsideration of claims 15 and 19.

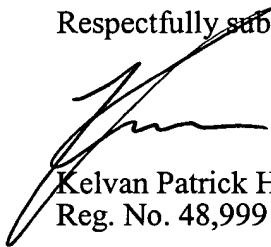
Applicant submits that the claims are now ready for allowance.

**Conclusion:**

Applicant has amended the specification to correct any misspellings. Applicant has amended claims 11, 12, 13, 15, 16, 18, and 19 using alternative language to avoid potential ambiguity and to clarify applicant's intended area of practice. The applicant has respectfully submitted a discussion of the cited references and requested withdrawal of the rejection of claims 11-20 under 35 U.S.C. 112, 102, 103, and the doctrine of obviousness-type double patenting. Reconsideration of pending claims 11-20 is respectfully requested. In view of the amendments and remarks set out above, it is submitted that this application is now ready for allowance.

If Examiner Yang believes that prosecution of this application can be expedited by discussion of any issue, she is invited to telephone the undersigned at any of the numbers set out below.

Respectfully submitted,



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